SYSTEMIC POISONS AND INCIDENTAL GASES

by

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The group of chemical agents which I have been asked to discuss may be encountered by the armed forces and also, under certain conditions, by the civilian population. Systemic poisons are breathed admixed with air, penetrate the epithelial lining of the lungs, pass into the blood stream and diffuse throughout the entire body. Any local action is either lacking or delayed and of secondary importance.

This group includes carbon monoxide, nitric fumes, hydrocyanic acid, arsine and hydrogen sulphide. The first three agents are of most importance. Cyanogen chloride and cyanogen bromide are usually considered in this group, while discussing hydrocyanic acid.

I. Carbon Monoxide. CO

Carbon monoxide is produced in any process where combustion of organic matter occurs in the absence of an adequate amount of air. It is a non-persistent gas and lighter than air. Military hazards include gun blasts, exploding shells, exhausts from motors of mechanized equipment, and stoves in dugouts with inadequate flues and ventilation, etc. The detonation of 1 kilogram of a modern high explosive produces from 600 to 800 liters of CO. The atmosphere around a bursting shell may attain a concentration of 40 to 60 per cent of carbon monoxide. This may constitute a hazard to an unprotected individual entering a confined space after an explosion. Little danger occurs in the open because of the lightness and ready diffusibility of this gas.

In civilian life the hazards are numerous. One has but to recall the recent tragic Cocoanut Grove Restaurant fire in Boston to realize the danger of being trapped in a burning building. In their report, of this catastrophy, Faxon and Churchill state (J.A.M.A. 120, 1385, 1942) "Some of the dead showed no burns; they had obviously been asphyxiated. Many showed the cherry-red color of carbon monoxide poisoning." Leaking gas mains, defective gas heating equipment, and improperly installed stoves take a toll of many lives annually. The CO content of illuminating gas ranges from 10 per cent in coal gas to 30 to 40 per cent in water gas. Stove cleaners in steel mills are subjected to CO poisoning unless removed to fresh air at frequent intervals.

Carbon monoxide is not directly toxic to the tissues. Its affinity for hemoglobin is 210 times greater than that of oxygen for hemoglobin. Poisoning is therefore due to an induced anemic anoxia as shown in the following slides:-

MECHANISM OF CO POISONING

Slide OCD 1

CO produces tissue anoxia
1st. CO + hemoglobin → carboxyhemoglobin
$CO + Hb \rightarrow HbCO$
HbCO unavailable for O_2 transport
Affinity CO for Hb is 210 X O_2 for Hb.
Thus - if conc. of CO in inspired air is only 1/210 that of O_2, the blood will contain equal amounts of HbCO and HbO_2.

[illegible]

[illegible]

[illegible]

[illegible]

1. Carbon monoxide, CO

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

CALCULATIONS:-

Air normally, 20.9% O_2 by volume
Therefore, 0.1% CO by volume
furnishes CO conc. of 1/210 that of O_2 content.
This is only 1 part in 1000 parts air.

Slide OCD 2

2nd. HbCO interferes with dissociation of O_2 from remaining HbO_2 and thus still further reduces amount of O_2 available to the tissues.

The presence of carboxyhemoglobin alters the dissociation curve of oxyhemoglobin in an unfavorable manner so that less oxygen is given up in the tissues. For example, the patient with CO poisoning, sufficiently severe so that 60 per cent of the normal hemoglobin content of his blood is inactivated, is considerably worse off than the patient who lacks 60 per cent of his normal hemoglobin quota as a result of anemia. Each has 40 per cent of hemoglobin for combination with O_2, but the patient with circulating carboxyhemoglobin does not release but roughly ½ as much oxygen in his tissues as the anemic patient. Such an individual is near the point of collapse, whereas, the anemic patient may show no marked symptoms.

The toxic effects of CO are therefore purely secondary to the tissue anoxia. While it is true that under very high CO tensions, cellular respiratory enzymes may combine with the gas, the concentrations capable of causing clinical poisoning are toxic only, by virtue of the formation of carboxyhemoglobin. Cellular respiration will continue in a normal manner if sufficient oxygen is supplied.

The symptoms of carbon monoxide poisoning require no discussion before this audience. The following slide correlates the blood saturation with subject's condition.

SYMPTOMS OF CO POISONING

Slide OCD 3

Slide OCD 4

Blood Sat'n.	Symptom
0 - 10%	None
10 - 20%	Tightness across forehead, possibly headache
20 - 30%	Headache, throbbing temples
30 - 40%	Severe headache, weakness, dizziness, dimness of vision, nausea, vomiting collapse.
40 - 50%	Above symptoms, collapse, syncope, increased pulse and respiration.
50 - 60%	Syncope, increased respiration and pulse, coma with intermittent convulsions.
60 - 70%	Coma, intermittent convulsions, depressed heart action and respiration, possible death.

Slide OCD 5 — 70 - 80% — Weak pulse, slowed respiration, respiratory failure and death.

(After Sayers and Davenport)

It is evident from the above that symptoms merge one with another, the severity increasing as concentration increases. Exposure to high concentrations, causes a rapid saturation of the blood. The victim under these conditions may experience only transient weakness and vertigo before unconsciousness occurs.

The two important factors governing the toxicity of carbon monoxide, are the concentration of gas in the inspired air, and the duration of exposure.

These relationships are shown in the following table:

CARBON MONOXIDE POISONING

Slide OCD 6

Effect	Air Contains Vol. %
Allowable for an exposure of several hours	0.01
Can be inhaled for one hour without appreciable effect	0.04-0.05
Causing a just appreciable effect after one hour's exposure	0.06-0.07
Causing unpleasant but not dangerous symptoms after one hour's exposure	0.1 -0.12
Dangerous for exposure of one hour	0.15-0.20
Fatal in exposure of less than one hour	0.4 and above

(Table after Jacobs)

Henderson and Haggard (1927) formulated the following simple rule for calculating the probable toxicity of inhaled air of known carbon monoxide content: This rule states that the product of the Exposure time in hrs. X Parts Co in 10,000 air.

If under 6, there is no danger to life
If product reaches 9, symptoms begin
If product reaches 15, life is endangered.

The application of this formula indicates that a concentration of 0.1 volume per cent (10 parts per 10,000) of gas could be tolerated without symptoms for 30 minutes, whereas a 90 minute exposure would be dangerous. The formula is applicable only to normal persons at rest. Children are more susceptable than adults, because of their higher metabolic rates. Anemic individuals are likewise more susceptable. Small animals, as mice and birds, because of their high metabolic rates, have been employed for the detection of toxic concentrations of carbon monoxide in mines, dugouts, etc. The air is safe for human beings as long as these animals remain unaffected.

Slide CO 3	70 - 10%	Weak pulse, slowed respiration, respiratory failure and death.

(After Haggard and Davenport)

It is evident from the above that symptoms occur with small amounts, the severity increasing as concentration increases. Exposure to high concentrations causes a rapid saturation of the blood. The patient under these conditions may experience only transient symptoms and may lapse into unconsciousness or coma.

The two important factors governing the toxicity of carbon monoxide, are the concentration of gas in the inspired air, and the duration of exposure.

These relationships are shown in the following table:

CARBON MONOXIDE POISONING

	Effect	Air Concentration Vol. %
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Slide CO 4	Causing a just appreciable effect after one hour's exposure	0.06-0.07
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The observed pathological changes are those resulting from anoxia. Cerebral capillary damage resulting in cerebral edema and areelevated intracranial pressure. This damage may explain the severe headache following CO intoxication. Cellular changes may occur in the brain, and permanent damage to the central nervous system result even if the victim recovers. The higher centers are more sensitive than the lower to oxygen deprivation. The heart and blood vessels may also be injured and cardiovascular as well as cerebral symptoms appear during the post-exposure period. Small hemorrhages in the brain, heart, and other organs, with perivascular infiltration and focal necroses have been observed in both experimental and clinical CO poisoning. The blood has a characteristic cherry-red color, due to carboxyhemoglobin.

The diagnosis of CO poisoning is often presumptive, from the circumstances under which the victim is found. The characteristic cherry-red cyanosis of the skin, mucous membrane and area under the fingernails, is pathognomic.

A simple method to establish the presence of CO in blood is the pyrotannic acid test. Normal blood when diluted with water and treated with a mixture of pyrogallic and tannic acids, gives a brownish-gray coagulum, whereas, blood containing CO gives a light carmine colored coagulum. The intensity of the carmine color is proportional to the degree of CO saturation. For medico-legal purposes carbosyhemoglobin should be determined in blood by an accepted chemical method.

Treatment of acute CO poisoning commences when the victim is removed from the contaminated atmosphere and placed in air. Persons effecting the rescue should be provided with an oxygen helmet or special canister, since the regular service mask affords no protection. The entire plan of treatment is based upon the dissociation of carboxyhemoglobin and its replacement by oxyhemoglobin. The following outline is taken from notes of Prof. Louis Goodman of Yale University:

THERAPY OF CO POISONING

Ordinary service mask - No protection
Object of therapy - Get adequate O_2 to tissues

1. Remove victim to pure air
2. Artificial respiration if necessary
3. Administer pure O_2 if available, because:

Slide OCD 7

   a) High O_2 tension hastens dissociation of HbCO

   b) High O_2 tension increases amount of O_2 dissolved in plasma (from 0.3cc. to 2.2 cc. per 100 cc. Blood), and allows 15% more O_2 to be carried by blood

Slide OCD 8

4. Better yet, administer 5% to 10% CO_2 in oxygen.
   a) CO_2 stimulates respiration, thus hastens elimination of CO

   b) CO_2 decreases the pH of blood, thus increasing the dissociation

of HbCO into Hb and CO.

Slide OCD 9

5. Give supportive therapy.
Keep patient warm
Prevent exertion, to keep O_2 needs at minimum.

DO NOT USE METHYLENE BLUE - ITS USE IS IRRATIONAL

The use of CO_2 and O_2 permits the body to expell all CO in about 30 minutes. The use of oxygen alone may require 30 to 90 minutes, and fresh air approximately 2 hours.

Goodman gives the following statement relative to methylene-blue therapy: "The dye was employed in the belief that it could serve in the place of tissue oxidases, poisoned by carbon monoxide. However, there is no evidence that methylene blue can function in this manner, there is no proof that tissue oxidases are in the least affected by carbon monoxide concentrations encountered in clinical poisoning, and even if the claims were true, the presence of carboxy-hemoglobin would prevent the possibility of sufficient oxygen reaching the tissue. Methylene blue is not entirely innocuous and is capable of converting hemoglobin to methemoglobin. By using this irrational therapy one would only be complicating one type of poisoning with another, and still further reduce the oxygen-carrying capacity of the blood. The sporadic clinical reports of success with methylene blue probably represent cases which recovered in spite of harmful therapy."

In view of the possibility of after-effects of severe CO-poisoning the prognosis should be guarded. If coma persists over an extended period, marked cerebral damage has probably occurred. Neurological and psychiatric disorders, tachycardia and dyspnea may continue for months.

II. Nitric Fumes (Nitrous Fumes)

Nitric fumes constitute both an industrial and a military hazard. They are produced in the pickling of metals, especially brass, the detonation of cordite or other high explosives, in industrial nitration plants, and whenever nitric acid comes in contact with organic material.

Published data show the breaking of carboys and other containers of nitric acid, to be the most common cause of fatal nitrous fume poisoning. Spilled acid should be washed away with large amounts of water, and never absorbed by sawdust or other organic material. Clean sand may be used as a cover if necessary.

One will recall the disastrous fire at the Cleveland Clinic some years ago in which casualties resulted from the inhaling of fumes from burning X-Ray Films.

The group of nitrous fumes includes the following chemical agents:

NITROUS FUMES

Slide OCD 10

Nitrous oxide, N_2O --------------- colorless anaesthetic
Nitric oxide, NO ----------------- colorless, toxic
Nitrogen dioxide, NO_2 ----------- reddish brown, toxic
Nitrogen tetroxide, N_2O_4---------- a colorless liquid polomer of NO_2

of MORE THAN 50 min. CO.

SLIDE NO 9
3. Stop unnecessary exertion.
Keep patient warm
Prevent shivering, as may be
needs of rewarming.
DO NOT USE STIMULANTS [illegible]
OF THE PATIENT.

The use of CO_2 and O_2 permits the body to rid itself of CO in about 30 minutes. The use of oxygen alone may require 30 to 40 minutes, and fresh air approximately 4 hours.

Drinker gives the following statement in relation to carbon-monoxide treatment. "It is the gas employed at the Central Park [illegible] carbon monoxide. However, there is no evidence that methylene blue [illegible] in this manner [illegible] by carbon monoxide [illegible] and even if the action be [illegible] methylene would [illegible] the possibility of [illegible] methylene blue [illegible] to [illegible] carrying capacity of the blood. [illegible]"

In view of the possibility of after-effects of severe CO-poisoning the prognosis should be guarded. If coma persists over an extended period, marked cerebral damage has probably occurred. [illegible] and [illegible] may complicate the recovery.

II. NITROUS FUMES (NITROGEN OXIDES)

Nitrous fumes sometimes occur in industrial and military spaces. They are produced in the handling of nitric acid, [illegible] or other high explosives, in industrial electroplating plants, and whenever nitric acid comes in contact with organic material.

Particular care must be exercised in [illegible] nitric acid, [illegible] the most common cause of [illegible]. Spilled acid should be [illegible] with large amounts of water, [illegible] never absorbed by sawdust or other organic material. Clean sand may be used as a cover if necessary.

You will recall the disastrous fire at the Cleveland Clinic some years ago in which many deaths resulted from the inhalation of fumes from burning X-ray films.

The group of nitrous fumes includes the following chemical species:

NITROUS FUMES

SLIDE NO 10
Nitrous oxide, N_2O ------ colorless anesthetic
Nitric oxide, NO ------ colorless, toxic
Nitrogen dioxide, NO_2 ------ reddish brown, toxic
Nitrogen tetroxide, N_2O_4 ------ colorless liquid polymer of NO_2

Nitrous fumes in the presence of moisture may also contain nitric (HNO_3) and nitrous (HNO_2) acids.

Nitrous oxide is a weak innocuous anaesthetic familiar to you all.

Nitric oxide does not exist as such in air, being converted to nitrogen dioxide. We are, therefore, concerned only with nitrogen dioxide (NO_2) and its polomer, nitrogen tetroxide (N_2O_4). The properties of nitrogen tetroxide are shown in the following table:

Properties of N_2O_4

	Colorless crystals at	-9.3°C
	Yellow liquid at	+10.0
	Yellow-red liquid at	15.0
	Darker yellow-red liquid at	20.0
	Boils, brown fumes at	21.3
	Completely volatilized at	22.0
Slide OCD 11	Chocolate brown vapor at	40.0
	Black vapor at	140.0

The composition of nitrous vapor is controlled entirely by temperature as shown in the next slide:

Composition of Nitrous Vapor
Color varies with temperature
Slide OCD 12 Temperature determines ratio:

Temp.	N_2O_4	NO_2
40°C.	70%	30%
60°C.	50%	50%
135°C.	0%	100%

From this data it is evident that regardless of the molecular form inhaled, the vapors are at once altered to correspond to the equilibrium for body temperature. At 40°C, approximately 30% exists as NO_2 and 70% as N_2O_4. These in the presence of water form nitric and nitrous acids.

The toxicity of nitrogen dioxide for man is shown in the following table:

TOXICITY OF NITROGEN DIOXIDE FOR MAN

(Lehmann and Hasegawa. 1913)

	Concentration Parts per million by volume	Symptoms
	(Self experiments of Hasegawa)	
Slide OCD 13	64	Moderate irritation of larynx, respiration slightly increased and shallow.
	100	Marked irritation of larynx, cough

207	Very marked irritation of nose and larynx, cough, increased nasal secretion and lacrimation
(Lehmann's conclusions)	
37	May be tolerated for several hours by many persons
74	May be tolerated for ½ hour
117-154	Dangerous with somewhat prolonged exposure
234-388	Rapidly increasing danger.

Few symptoms are evident at low concentrations. The maximum allowable concentration is 37 to 39 parts per million of air. According to Goodman, the main effects observed below this critical concentration are those resulting from the absorption of sodium nitrite which is produced by the action of nitrous acid in the alkaline tissue fluids. Approximately 20 milligrams of $NaNO_2$ may be formed in the lungs and absorbed during 1 hour's exposure to a maximum allowable concentration of nitrous fumes. The symptoms observed, therefore, are characteristic of the nitrite ion, namely, hypotension, headache, giddiness. Some methemoglobin formation occurs. Men frequently exposed to low concentrations of nitrous fumes, may acquire a tolerance to the nitrite ion. They are still susceptible to the irritant effects of the acids on the respiratory tract.

Higher concentrations of nitrous fumes produce marked local irritation of the broncho-respiratory tract. Pulmonary edema occurs, and local ulceration of the bronchi or lungs may result from nitric acid.

Frequently, an asymptomatic interval of from 4 to 18 hours may follow inhalation of toxic concentrations of nitrous fumes. Slight irritation of the eyes, nose and pharynx are noticeable. Symptoms similar to those of phosgene poisoning may then appear.

Because of the asymptomatic period, the victim may not realize that he has been seriously gassed and returns to work instead of remaining at rest and under treatment. Rapid fatalities occur when the concentration of nitrous fumes approximate 500 parts per million of air.

The diagnosis of nitrous fume poisoning is based upon the history of the exposure, the irritation to eyes, nose and throat, the pungent odor, and with high concentrations, the discoloration of the mucous membranes.

Protection against nitrous fumes is afforded by the service canister. Therapy is symptomatic and similar to that for phosgene poisoning. The prognosis is not good once pulmonary edema has developed. Casualties usually die within 24 to 48 hours. A fatal broncho-pneumonia may complicate a case which apparently is recovering from pulmonary edema. Convalescence is prolonged.

Victims exposed to nitrous fumes may also have been simultaneously exposed to other gases especially carbon monoxide. The thermal decomposition of 100 grams of celluloid, for example, furnishes 4 to 7 liters CO and about the same amount of nitrogen dioxide. Symptoms of carbon monoxide poisoning may therefore dominate the clinical picture.

III. Hydrocyanic Acid. "Vincennite"

Poisoning by cyanide is usually due to hydrocyanic acid or its salt, potassium cyanide. Acids, as weak as carbonic will liberate HCN from its salts. For this reason, inhaling of air from a container partly filled with KCN, may cause an undesirable systemic reaction. All compounds which release the cyanide ion, have the same mechanism of systemic action, and the principles of treatment are the same.

The military use of HCN has not as yet been very extensive. During 1915, in World War I, the French filled shells with hydrocyanic and phosgene, but hesitated to authorize their use. These were, however, used in the battle of the Somme, July 1, 1916. The Germans suffered but slightly, since they had learned of the contemplated use of HCN by the French a week before its introduction at the front, and had equipped their troops with special mask filters containing 1 gram of pulverized silver oxide scattered through the potash layers. This afforded adequate protection.

Most civilian cases of cyanide poisoning are those with suicidal intent. Because of its rapidity of action, hydrocyanic acid has been adopted by several states for use in executing criminals.

Pure hydrocyanic acid is a colorless liquid. It boils at 26°C., yielding a vapor which is 0.93 as heavy as air. It has a faint odor resembling bitter almonds. The vapor is exceedingly volatile (873 mg. per liter at 20°C.) and persists in the open only a few minutes after release. Because of the rapid diffusion of this gas, military use required its admixtures with stannic chloride and arsenic trichloride. Chloroform is also added to prevent polymerization.

It cannot be denied that if cyanide can be released in battle in effective concentrations, (a condition which might be realized in dugouts, deep trenches, aboard ships, and within tanks, etc.) it will produce toxic or lethal effects with dramatic rapidity, (thereby avoiding the destruction of desirable equipment).

The cyanide ion acts on the respiratory ferments of the tissue cells, preventing them from taking up oxygen. Death is due to an histotoxic anoxia, which is an asphyxia, in the presence of normal amounts of oxygen. It is reminescent of the old adage - "Water, water everywhere, but not a drop to drink."

With tissue utilization suspended, there is less than the normal difference between the oxygen content of arterial and venous blood. The carbon dioxide content, of venous blood, is likewise close to that of arterial blood. Cyanosis does not appear until the beginning of respiratory failure.

It will be recalled that in very low concentrations, the cyanide ion acts upon the chemoreceptors of the carotid body, producing indirectly through the medulla an intense stimulation of respiration. This action is transcient in character.

In cyanide poisoning the cells of nervous tissue are early affected because of their sensitivity to oxygen want.

The following material relative to cyanide toxicity and therapy is taken largely from Goodman.

The cyanide ion is detoxified in the body by combination with sulfur to form non-toxic sodium thiocyanate which is excreted by the kidney. The ability of the tissues to detoxify cyanide is definitely limited. When the ion reaches the circulation more rapidly than it can be disposed of, cumulative poisoning quickly ensues, resulting in death. If air containing less than the critical concentration of 0.03 mgm HCN per liter (3 parts per 100,000) is breathed, the detoxification mechanism, by conversion to thiocyanate, is adequate. Above the critical concentration, the rapidity of poisoning, depends upon the concentration inhaled and the time of exposure. The lethal concentration is

0.2 mgm. per liter for 10 minutes exposure,

and 0.15 mgm. per liter for 30 minutes exposure.

Injection of 50 mgm. under the skin is lethal.

The symptoms of cyanide poisoning depend in character and severity on the concentration of the inhaled gas. With high concentrations, a few inhalations result in unconsciousness and death with a few minutes. With low concentrations, the symptoms develop more slowly. They include weakness, giddiness, hyperpnea, headache, palpitation and nausea with salivation. Cyanosis and unconsciousness then ensue, and terminal asphyxial convulsions are common.

The therapy of cyanide poisoning must be heroic and given rapidly to be effective. According to Goodman, the most recent and best treatment consists in the intravenous use IN SEQUENCE of sodium nitrite and sodium thiosulfate. The cyanide ion does not combine with hemoglobin, but does combine rapidly with methemoglobin. This affords a means of quickly removing the highly toxic cyanide ion from the circulation by converting it to cyanmethemoglobin which is non-ionized and non-toxic. The method employed to obtain a methemoglobin is the injection of $NaNO_2$. The nitrite ion quickly converts hemoglobin to methemoglobin. The cyanide ion is slowly released from cyanmethemoglobin and is then converted to the non-toxic thiocyanate. This last-named reaction is insured and perhaps accelerated by the presence of injected thiosulphate.

The following tables taken from Goodman, summarize these points:

MECHANISM OF CYANIDE TOXICITY

Slide OCD 14

$\bar{CN}$ poisons the respiratory mechanism of tissue cells by combining with iron-containing respiratory ferments.
DEATH is due to tissue anoxia and failure of the medullary respiratory center.

RATIONALE OF THERAPY

Slide OCD 15

$\bar{NO_2}$ + Hb --) METHb (Rapidly formed)

CN + METHb --) CYANMETHb (Non-ionized non-toxic)

CYANMETHb --) CN^- (Slow dissoc.)

NaTHIOSULPHATE + CN^- -- Na THIOCYANATE
($Na_2S_2O_3$) NaCNS (Non-toxic)

THERAPY OF CYANIDE POISONING

Slide OCD 16

Remove patient to fresh air. DO NOT ENTER GASSED AREA WITHOUT A MASK. If heart beats, start intravenous therapy.

Step 1. Inhalation of amyl nitrite (30 seconds out of each 2 minutes) while 3% $NaNO_2$ solution is being prepared. (Nitroglycerine is effective). In oral poisoning, wash out stomach in this interval.

Step. 2. Inject intravenously 10 cc. of 3% $NaNO_2$ solution (0.3 gm.) Take 3 or 4 minutes for injection.

Slide OCD 17

Step 3. Inject 50 cc. of a 50% $Na_2S_2O_3$ solution (25 gms.) Take 10 mins. for injection.

Step 4. Watch patient closely for 24 to 48 hours.

Slide OCD 18

If symptoms recur, repeat steps 2 and 3, using half doses. If alarming hypotension occurs from the nitrite, epinephrine or ephedrine may be used. If anoxia from too much methemoglobin, inhalation of 100% oxygen may be necessary, or even blood transfusion.

Approximately 20 lethal doses of cyanide have been antidoted in experimental animals by the treatment suggested above. Its comparison with other methods of treatment is given in the following table:

Slide OCD 19

Treatment	No. M.L.D's Required to kill dog.
None	1
Nitroglycerine	1
Methylene blue	3
Na thiosulphate	4
Na tetrathionate	4
Amyl Nitrite	5
$NaNO_2$	5
Methylene blue and Na tetrathionate	7

	Amyl Nitrite and Na thiosulphate	11
	$NaNO_2$ and Na tetrathionate	14
Slide OCD 20	$NaNO_2$ and Na thiosulphate	21

If the patient survives an hour, recovery generally occurs. After effects are rare. Mortality rate from acute cyanide poisoning is very high.

The isonitrites, cyanogen bromide and cyanogen chloride, produce the systemic toxicity of cyanide and also act as lacrimators and pulmonary irritants.

IV. Arsine Poisoning AsH_3

Arsine is a colorless gas, heavier than air, inflammable, has a garlic-like odor and metallic taste. The last two properties are attributed to accompanying impurities. Arsine is liberated with hydrogen when an acid acts on a metal, if either the acid or metal contain arsenic. The Marsh Test for arsenic is a familiar application of this principle. Arsine may be liberated from industrial wastes, as for example, wastes from chemical plants making sulphuric acid from arsenic containing pyrites.

Arsine has not as yet been employed as a war gas. Storage battery gases, or waste tanks on ships, may theoretically constitute military hazards.

The extreme toxicity of arsine for man is shown in the following table:

Toxicity of AsH_3 For Man

Parts AsH_3 per 100,000 air.	Time breathed	Comment
250	30 minutes	Fatal
50	60	Dangerous
30	Several hrs.	Mild symptoms
Highly-concentrated	Few whiffs	Fatal

The service canister affords adequate protection against arsine.

Arsine when inhaled, enters the blood and combines with hemoglobin. It is gradually changed to a toxic arsenical compound of unknown nature. It may be an oxidation product. This toxic compound causes the hemolysis of the red blood corpuscles. Arsine has also a direct depressant action upon the central nervous system.

The following table shows the rapid fall of erythrocytes in dogs gassed for 30 minutes with a concentration of 0.53 mgm. arsine per liter of air. (53 parts in 100,000,000 air)

BLOOD CHANGES FOLLOWING GASSING WITH ARSINE

		Erythrocytes		Leucocytes
	Before gassing	6,530,000		22,400
	Time of gassing	5,800,000		20,200
	6 hrs. after gassing	3,480,000)		12,800
	1st day	2,660,000)	Hema-	23,200
	2nd day	2,450,000)	turia	25,400
Slide OCD 21	3rd day	2,300,000)		70,000
	4th day	2,260,000)		66,500
	5th day	2,570,000		54,800
	10th day	3,750,000		15,600
	15th day	4,060,000		15,800
	24th day	5,010,000		14,800

Hematuria appeared 6 hours after gassing and continued for 4 days. Other symptoms include diarrhea, tarry stools, marked weakness and depression. Eventually recovery was complete.

Pathological changes observed in arsine poisoning are mainly secondary to the acute hemolytic crisis. Marked destruction of erythrocytes, enlargement of the spleen and liver and jaundice are present. Hemoglobin is precipitated in the tubules of the kidney. The blood picture, urinary findings and serum bilirubin are the same as occur in any severe hemolytic anemia.

The symptoms of arsine poisoning depend in severity upon the concentration of the gas and the duration of exposure. They may be delayed from 6 to 36 hours following gassing.

Death may occur in severe poisoning before symptoms can appear, while mild cases may show only lassitude, headache, mild dyspnea, a rapid pulse, followed somewhat later by a slightly yellowish tinge to the skin. In the average case the outstanding symptoms are chills, fever, severe myalgia, nausea and vomiting, lumbar pain. The urine is scanty, deep-brown or red in color, contains free hemoglobin, bile pigments, red cells, albumin and casts. Jaundice usually develops on the second day. Symptoms of anemia and anoxia are present. The patient is weak and exhibits dyspnea.

Evidence of the depressant action of the gas on the central nervous system may be noted in the early phases of the poisoning. The blood picture is typical of an acute hemolytic crisis. Complete anuria with uremia may result from the mechanical blockage of the renal tubules, by the precipitation of free hemoglobin in that portion of the tubule where the urine becomes acid. The blood contains free hemoglobin, also methemoglobin. A slatey cyanosis may therefore precede the jaundice. The clinical laboratory findings are similar to those observed in phenylhydrazine poisoning, black-water fever, paroxysmal hemoglobinuria, or acute hemolytic anemia from sulfonamides, etc. Death may occur between the third day and the end of the week.

In patients surviving the acute phases, subacute arsenical poisoning may occasionally be evident, particularly a peripheral neuritis. Other aspects of subacute arsenical poisoning are diarrhea, dermatitis, pigmentation, edema especially of the lower lids and ankles, and arsenical hepatitis and nephritis.

Recovery requires 4 to 6 weeks. Marked anemia and anuria are grave signs but victims may survive. About 30 per cent of the cases are fatal.

The main problem in diagnosis is the differentiation of arsine poisoning from other syndromes characteristic of acute hemolytic crisis. Test the urine for arsenic.

Treatment starts with the removal of the victim to fresh air. Therapy is symptomatic and designed to combat the anemia and impaired renal function. If anoxia is severe, oxygen inhalation may be indicated. Repeated blood transfusions may be given. Ample fluids are given in an attempt to promote diuresis. The urine should be kept alkaline to minimize the blocking of the kidney tubule by hemoglobin. Continue liberal amounts of alkalies until the urine no longer contains free hemoglobin.

Intravenous glucose, a carbohydrate rich diet, low in protein and fat is advisable if hepatitis is prominent. Iron salts and a nutritious diet are given during convalescence to promote blood regeneration. The use of sodium thiosulphate to promote excretion of arsenic is problematical.

V. Hydrogen Sulphide

Hydrogen sulphide, although briefly employed in World War I offers little prospect of military importance during the present conflict. It has several undesirable tactical features, and is easily detected by its characteristic odor, and readily absorbed by several types of canisters.

Its properties are known to you all. It is highly toxic, a concentration of 0.07 per cent (7 parts in 10,000) in inhaled air will cause death after an exposure of 30 minutes. The limit of danger for prolonged exposure is said to be a concentration of 50 parts per million.

The gas is encountered in chemical laboratories, the manufacture of sulphur dyes and of rayon, the refining of petroleum, the manufacture of coal gas, and also in sewer gas.

The symptoms of hydrogen sulphide poisoning other than those locally produced are due to the action of the gas upon the central nervous system. When inhaled in low concentrations, the patient suffers from headache, nausea, dyspnea, vertigo and marked malaise. Higher concentrations first stimulate, then depress the central nervous system. Stimulation may be sufficient to cause hyperpnea and convulsions. Eventually the respiration is depressed and death results from respiratory failure, with the heart beat continuing for several minutes.

Hydrogen sulphide is converted by the moist lung to sodium sulphide. In the blood stream this substance is oxidized to harmless sodium sulphate. This osidative process is said to deprive the tissues of needed oxygen. This is said to be the only mechanism by which the gas can cause an anoxia. It is denied that H_2S reacts with hemoglobin forming sulfhemoglobin. It has been established that H_2S combines only with methemoglobin, which normally is not present in the circulating blood. Methemoglobin is formed after death, and any H_2S formed from putrifaction of the intestinal contents will then combine to form sulfmethemoglobin. The bluish-green discoloration seen around the intestinal vessels of cadavers is formed in this way.

Prognosis: Recovery requires 4 to 6 weeks. [illegible] of [illegible] are [illegible] but victims may [illegible]. About [illegible] of the [illegible].

The main problem in diagnosis is the differentiation of arsine poisoning from other conditions characteristic of acute hemolytic anemia, from the [illegible] anemias.

Treatment should start with the removal of the victim to fresh air. Therapy is supportive and designed to combat the anemia and [illegible] renal shutdown. If anuria is severe, peritoneal dialysis may be indicated. Exchange blood transfusions may be given. Whole blood is given in an attempt to promote diuresis. The urine should be kept alkaline to minimize the deposition of the [illegible] in the kidneys. Continued liberal amounts of alkaline [illegible] until the urine no longer [illegible].

Preventive measures, a respirator with fresh air, if [illegible] of [illegible] is [illegible]. [illegible] masks and a self-contained [illegible] are [illegible] warning [illegible] of [illegible].

9. Hydrogen Sulphide

Hydrogen sulphide, although not [illegible] as a war gas, [illegible] military importance [illegible]. It is [illegible] chemical [illegible], and is [illegible] of [illegible].

The properties are [illegible]. It is [illegible]. A concentration of 0.07 per cent (7 parts in 10,000) is [illegible] on exposure of [illegible] minutes. The limit of danger for prolonged exposure is said to be a concentration of 20 parts per million.

The gas is encountered in chemical laboratories, the manufacture of [illegible], the [illegible] of petroleum, the [illegible] of coal gas, and [illegible].

The [illegible] of hydrogen sulphide poisoning [illegible] locally [illegible] are due to the [illegible] of the gas upon the central nervous system. [illegible] by the [illegible], the patient [illegible] from headache, nausea, [illegible], and [illegible]. Higher concentrations first stimulate, then depress the central nervous system. [illegible] and [illegible]. [illegible] the [illegible] with the [illegible], the [illegible].

Hydrogen sulphide is converted in the blood [illegible] sulphide. In the [illegible] this substance is [illegible]. This [illegible] is [illegible]. It is [illegible] that [illegible]. [illegible] in the [illegible]. [illegible] of [illegible] after [illegible] will [illegible]. The [illegible] in [illegible] the [illegible] of [illegible] in [illegible].

The following table presents data on the effects following inhalation of air containing H_2S.

EFFECTS OF HYDROGEN SULFIDE

Concentration of Air		Effects
Parts by volume	Mg. per liter	
1 in 2000	0.76	Very dangerous if inhaled for 15 to 30 minutes. Causes severe irritation of the eyes and respiratory tract with risk of pneumonia or serious injury to the lungs, which may readily prove fatal.
1 in 5000	0.304	Dangerous if inhaled for one hour. Causes severe irritation of the eyes and respiratory tract. Eyes are affected after 6 to 8 minutes.
1 in 10,000	0.152	Symptoms of local irritation of eyes and respiratory tract after one hour's exposure

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Table from Jacobs "War Gases"

An adjunct to the diagnosis of H_2S poisoning is the blackening of a moistened silver coin or moistened lead acetate paper by the victims breath.

Treatment commences with the removal of the victim to fresh air. If still breathing administration of O_2 and CO_2 is helpful. If respiration ceases, institute artificial respiration using O_2 and CO_2 as long as the heart continues to beat.

If respiration and tissue oxygenation can be maintained the body oxidizes the H_2S to non-toxic Na_2SO_4.

Pneumonia may follow in severe cases.

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In preparing this lecture extensive use has been made of the material prepared for a similar lecture by Dr. Louis Goodman of Yale University.

Acknowledgment is also made for material taken from the following sources:

Medical Aspects of Gas Warfare ---------- Ireland, 1926
War Gases ------------------------------- Jacobs
Chemicals in War------------------------- Prentiss
The Toxicity and Potential Dangers of
Nitrous Fumes, Public Health Bulletin, No. 272
Various other Government Publications.

The following table presents data on the [illegible] following [illegible] treatment of [illegible], 1947:

[illegible]

Concentration of [illegible]		Effects
Parts by volume	Gm. per liter	
1 in 2500	0.75	[illegible]
[illegible]		
1 in 5000	0.304	[illegible]
1 in 10,000	0.152	[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

Acknowledgment:

[illegible]

[illegible]

[illegible] ---------- [illegible], 1942
[illegible] ----------
[illegible] ---------- [illegible]
[illegible]
[illegible], Bulletin, No. 372
[illegible] Government Publication.